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| 09/429,798      | 10/29/1999  | NNOCHIRI N. EKWURIBE | 4012-113DIV1        | 6336             |

7590 08/12/2004

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| EXAMINER |
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AUDET, MAURY A

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| ART UNIT | PAPER NUMBER |
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1654

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/429,798

Applicant(s)

EKWURIBE ET AL.

Examiner

Maury Audet

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 73-86 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 73-86 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 11/19/2003.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election, with traverse of Group I, as drawn to a conjugate of non-naturally occurring opioids as a therapeutic compound and an oligomer of a general formula, in the paper filed May 18, 2004 is acknowledged. Applicant has not provided any grounds for the traversal of the restriction requirement. This is not found persuasive, and the election to the restriction requirement is thus treated as without traverse.

The restriction required that Applicant elect a specific conjugate as the invention, and that this requirement was not to be taken as an election of species, but rather as an election of the invention. Applicant has stated on the last page of the response ("Remarks") that the Examiner agreed to treat both the therapeutic compounds and the oligomer formula as species within the claimed conjugate. The Examiner does not recall opening the search and examination to *any* species of either compound within the conjugate.

Thus, the original requirement, that Applicant elect as single conjugate, is still deemed proper and is therefore made FINAL.

However, in order to move prosecution along, the Examiner is willing to search the oligomer of broad claim 1 as drawn to a therapeutic agent of SEQ ID NOS: 1 or 48; the only distinctly claimed/searchable opioid(s) (Applicant's therapeutic agent election), and thus searchable conjugate.

Accordingly, claims 73-86 have been searched and examined on the merits only insofar as being drawn to a conjugate of claim 73, wherein the therapeutic agent within the conjugate is the opioid of SEQ ID NOS: 1 or 48.

***Claim Rejections - 35 USC § 112 1<sup>st</sup> Scope***

Claims 73-86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for opioid-oligomer conjugates consisting of SEQ ID NOS: 1 or 48, as drawn to the broad formula of claim 1; does not reasonably provide enablement for any and all opioids/compounds as therapeutic agents within the claimed conjugate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)).

Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988)). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for any and all conjugates comprising any opioids/compounds as the therapeutic agents within the claimed conjugate of the broad formula of claim 1.

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*The nature of the invention:* The invention is drawn to oligomer conjugates of the broad formula of claim 1, wherein any therapeutic compound (for instance peptide opioids) may be conjugated to the oligomer therein.

*The state of the prior art and the predictability or lack thereof in the art:*

Amino acids range from common amino acids, to uncommon amino acids, and even "important amino acids, such as the neurotransmitter  $\gamma$  aminobutyric acid, that have no relation to proteins." (Online-Medical Dictionary. "Amino acid". <http://cancerweb.ncl.ac.uk/cgi-bin/omd?query=amino+acid>. 13 Nov. 1997).

*The amount of direction or guidance present and the presence or absence of working examples:* Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification describes that any therapeutic compound/opioid may be conjugated to the oligomers of the broad formula of claim 1. However, the only therapeutic agents (i.e. elected opioids) distinctly claimed are SEQ ID NOS: 1 and 48.

*The breadth of the claims and the quantity of experimentation needed:* The claims are drawn broadly to oligomer conjugates of the broad formula of claim 1, wherein any therapeutic compound (for instance peptide opioids) may be conjugated to the oligomer therein. With the substantial variability among what amino acids may be encompassed in the broad range of peptide opioids (including synthetic opioids, and what undefined substitutions therein) capable of functioning within the invention;; it is not clear as to what may be included (i.e. what opioid peptide structures/amino acid residues) in the invention as claimed. Absent sufficient teachings in the specification or art sufficient to overcome the teachings of unpredictability in the art as to enablement on the

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use of any opioid (or other therapeutic agent for that matter); it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

***Claim Rejections - 35 USC § 112 2nd***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 73-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 73, it is unclear what the invention is, based on the broad claim language to any therapeutic compound within the broad oligomer formula of claim 73. To hasten prosecution (including so as to avoid potential further restriction requirements), it is strongly suggested that Applicant amend the claims to be drawn to the oligomer of broad claim 73 conjugated to the opioid SEQ ID NOS: 1 and 48.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

***Allowable Subject Matter***

The elected, examined invention (i.e. a drug-oligomer conjugate comprising the conjugate of claim 73 and an opioid of SEQ ID NOS: 1 or 48) is free of the art or record. The prior art of record does not teach or reasonably suggest such a conjugate.

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*Conclusion*

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA  
8/8/04



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PRIMARY EXAMINER